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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,184	02/12/2001	Howard Sands	12636-898	6040

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	19

DATE MAILED: 10/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/782,184	SANDS ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of Corrected Drawings, Terminal Disclaimer, and Amendment C received on July 22, 2003 is acknowledged. Claims 1-36 are pending in this application.

Double Patenting

Claims 19 and 34-36 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,509,027 (Pub No. 2002/0142048) is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The phrase "pharmacologically acceptable lipophilic liquid vehicle with at least one membrane-forming lipid" does not have support in the specification as originally filed. The originally filed specification only has support for lipophilic vehicle. If applicant does contend there is support for the amendment, it is requested that the applicant clearly identify the page and lines in the specification that lends support to the amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "pharmacologically acceptable lipophilic liquid vehicle with at least one membrane-forming lipid" in all independent claims is vague and indefinite. It is unclear whether the membrane-forming lipid is the same as the outer layer phospholipid or a different lipid? Further clarification is requested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haynes (4725442) by itself or in view of Burke (5552156).

Haynes discloses microdroplets (200 angstroms up to a micron) of water insoluble drugs containing a pharmaceutically acceptable liquid surrounded by a layer of phospholipid, which are suitable for injection (Note the abstract, columns 2-8, and claims). Haynes discloses phospholipids, cholesterol, etc are utilized as the membrane-forming lipid (col. 5 and 6, line 56 to line 50). Although Haynes discloses his invention using anesthetics in examples, according to the reference, the composition can be used

to deliver any water insoluble/oil soluble drug via injection (col. 1, lines 26-39). The reference teaches the use of alkanes, fluorocarbons, natural plant derived oil, etc. for the organic phase. See column 5, lines 9-55. Haynes further teaches anti-cancer agents as the drugs which can be practiced in his invention (note col. 8, lines 27-28 and claim 15).

Hayes does not specifically teach camptothecins as the anti-cancer drug.

Burke teaches camptothecin drugs encapsulated by lipids to overcome the insolubility and instability problems of camptothecin for intravenous administration. Burke further discloses that the lipid encapsulation creates an internal environment with a low pH to prevent hydrolysis of camptothecin drugs. (Note abstract)

It is deemed obvious to one of ordinary skill in the art to use any hydrophobic drug including camptothecins, known in the art as a hydrophobic anticancer drug, with a reasonable expectation of success since Haynes provides the general guidance to prepare the compositions. One would be motivated to do so since Haynes suggests the incorporation of anticancer drugs into the formulation.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to encapsulate camptothecins in Haynes's phospholipid layers. One would be motivated to do so since Burke teaches the advantages of encapsulating camptothecins in phospholipid structures to successfully deliver instant cancer drugs by overcoming instability and insolubility problems.

Claims 9-11 and 18-36 ar rejected under 35 U.S.C. 103(a) as being unpatentable over Haynes (4725442) cited above or in combination with Burke cited above, further in view of WO 99/61001.

As set forth above, Haynes discloses microdroplets (200 angstroms up to a micron) of water insoluble drugs containing a pharmaceutically acceptable liquid surrounded by a layer of phospholipid (Note the abstract, columns 2-8, and claims). Although Haynes discloses his invention using anesthetics in examples, according to the reference, the composition can be used to deliver any water insoluble/oil soluble drug via injection (col. 1, lines 26-39). Haynes further teaches that anticancer agents can be practiced in his invention (note col. 8, lines 27-28). As also pointed out above, Burke teaches claimed camptothecins encapsulated in a lipid structure.

Haynes and Burke do not teach the inclusion of sugars such as mannitol or trehalose. The references also do not explicitly teach that the phospholipid-coated material can be sterilized.

WO 99/61001 discloses suspensions of submicron and micron sized particles of water insoluble biologically active substances containing lipoid and surface modifiers, phospholipids. The reference also teaches that sugars such as trehalose and mannitol are thermoprotecting agents and should be included for protection during sterilization (note the abstract, examples and claims). The reference also teaches the use of Lipoid E80 (Table 1).

The inclusion of sugars such as trehalose or mannitol in the compositions of Haynes or Haynes and Burke would have been obvious to one of ordinary skill in the art

at the time the invention was made. One would be motivated to do so since WO teaches that the instant sugars are thermoprotectants and protect the phospholipid particle suspensions during sterilization.

Response to Arguments

Applicant argues that the instant invention includes a substantially water-insoluble, pharmacologically acceptable lipophilic liquid vehicle having at least one membrane forming lipid, a camptothecin, and an outer layer of phospholipid. It is argued that the prior art does not disclose this.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points out that the claims have been rejected under 112 first and second paragraph and thus are interpreted in light of the specification. The specification points pout that the pharmaceutically acceptable vehicle may be vegetable oils, alkanes, fluorocarbons, etc. See page 27 of instant specification. These lipids are clearly taught by Hayes on column 5. Secondly when these lipids are mixed with water, they tend to aggregate and form droplets in the aqueous solution. Thus, this reads on membrane forming lipid. Hayes teaches the use of encapsulating the drugs in a phospholipid outer layer. Hayes further teaches the use of anti-cancer drugs. The secondary reference is relied upon to teach the instant anti-cancer drug.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SSG
9/29/03

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600